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Intramolecular Nicholas reactions in the synthesis of dibenzocycloheptanes. The synthesis of alcololchicine NSC 51046 and analogs, and the formal synthesis of (-)-alcololchicine.

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The preparation of dibenzocycloheptyne-Co$_2$(CO)$_6$ complexes by intramolecular Nicholas reactions of biaryl-2-propargyl alcohol-Co$_2$(CO)$_6$ derivatives is described. Reductive decomplexation of the dibenzocycloheptyne-Co$_2$(CO)$_6$ complexes affords the corresponding dibenzocycloheptenes, individual members of which have been employed in a formal total synthesis of (-)-allocolchicine, the preparation of 6,7-dihydro-3,4,9,10,11-pentamethoxy-5H-dibenzo[a,c]cyclohepten-5-one, and the enantioselective total syntheses of NSC 51046 and its 3,8,9,10-tetramethoxy regioisomer.

**Introduction**

The allocolchicines are a group of compounds containing a tricyclic 6,7,6-system with a highly oxygen substituted A ring. Individual members of this group, including (-)-allocolchicine (1), N-acetylcolchicinol methyl ether (NSC 51046, 2), N-acetylcolchicinol (3) and its dihydrogenphosphate (ZD 6126, 4) have gained considerable attention by virtue of having been found to be active against a number of cancer cell lines.

These act by inhibiting tubulin assembly and polymerization, therefore arresting cell mitosis. A number of additional naturally occurring allocolchicines, including (-)-androbiphenyline (4), (-)-colchibiphenyline (5), (-)-jerusalemine (6), (-)-salimine (7), and (-)-suhailamine have also been isolated; the latter two of these have undergone structural revision or are structurally in question.
Figure 1. Common allocolchicines.

Synthetic access to the allocolchicines historically has been based on oxidation of colchicine itself, although racemic syntheses or those involving resolution are known. More recently, the activity of these compounds has stimulated an interest in the enantioselective synthesis of allocolchicines. Initiated by Wulff’s Diels-Alder based synthesis of (-)-allocolchicine itself, members of this class of compounds have seen synthesis by way of enyne metathesis/Diels-Alder reactions ((-)-N-acetylcolchicine analogs), oxidative coupling and copper mediated cross coupling ((-)-N-acetylallocolchicinol), C-H activation reactions ((-)-allocolchicine formal synthesis), and aldol condensation chemistry ((-)-N-acetylallocolchicinol). In addition, a recent siloxane coupling/ring expansion reaction chemistry approach to (±)-NSC 51046 has been reported.

The application of alkyne-Co$_2$(CO)$_6$ complexes in the synthesis of seven-membered ring compounds has been demonstrated by our group and by other groups, most often based on Nicholas
reaction chemistry. The reactions are suited to seven membered ring synthesis due to fact that complexation of alkynes to \( \text{Co}_2(\text{CO})_6 \) induces a change in bond angle to ca. 140°,\(^{14}\) in that S\(_n\)1’ reactivity on the cationic propargyldicobalt complex to give a 5- membered ring system does not occur, and since the electrophilicity of these cations is such that arenes substituted with electron donating groups are sufficiently nucleophilic for facile reaction.\(^{15}\) In particular, given the propensity of propargyldicobalt cations for reaction with electron rich arenes and the demonstrated ability of (Z)-arylalkene substituted propargyl acetate complexes to react to form benzylocycloheptyne-Co\(_2(\text{CO})_6\) complexes,\(^{12d}\) we considered the potential applicability of intramolecular Nicholas reaction chemistry to dibenzocycloheptanes and consequently allocolchicines to be highly promising. We have reported on the viability of this approach in preliminary form, and now describe this chemistry in complete fashion.\(^{16}\)

**Results and Discussion**

The general outline of the access to the 6-7-6 system was envisioned to occur by construction of the \( \text{Co}_2(\text{CO})_6 \) complexes of biaryl-2-propargyl alcohol derivatives (8), which would deliver dibenzocycloheptyne-Co\(_2(\text{CO})_6\) complexes (9) in the presence of a Lewis acid. The former were prepared in most instances by Suzuki-Miyaura coupling reactions of arylboronic acids (10) with bromobenzaldehydes (11) according the conditions employed by Fürstner,\(^{17}\) giving biaryl-2-carboxaldehydes (12a-f) in good yield (Scheme 1, Table 1). These aldehydes were subjected to the Corey-Fuchs protocol, with trapping of the resulting acetylide by paraformaldehyde (Scheme 2). The resultant propargyl alcohols (13a-f) were formed in fair to good yields (56-80%) except in the case of thienyl substituted 13d (40% yield); in this case a significant amount of carbene insertion product 14 (53%) was formed competitively. Acetylation of 13a-f under standard conditions and complexation with Co\(_2(\text{CO})_6\) then afforded 8a-f in good to excellent yields.

**Scheme 1.** Suzuki-Miyaura coupling reactions.
Scheme 2. Preparation of Biaryl-2-propargyl Acetate-Co\(_2\)(CO)\(_6\) Complexes (8).

Table 1. Preparation of 8a-g

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<th>10</th>
<th>11</th>
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<td>10c</td>
<td>11a</td>
<td>12d</td>
<td>13d</td>
<td>8d</td>
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Two additional substrates were prepared by procedures other than the standard one. Unsubstituted 8g was obtained by way of Sonogashira reaction between 2-iodobiphenyl and propargyl alcohol to give 13g (87% yield) (Scheme 3), which was in turn subjected to acetylation and complexation with Co$_2$(CO)$_8$ under conditions analogous to 13a-f, affording 8g in 86% yield.

**Scheme 3.** Formation of 8g.

Carbomethoxy- substituted 8h, the propargyl ether-Co$_2$(CO)$_6$ complex envisioned as the precursor to allocolchicine itself, required a modified approach for its preparation. In this case, methyl 4-bromo-3-iodobenzoate, prepared by conventional esterification of the corresponding acid,$^{18}$ was subjected to Sonogashira reaction with propargyl methyl ether to afford 15 in 92% yield (Scheme 4). The Suzuki-Miyaura reaction of this halide with 2,3,4-trimethoxyboronic acid was somewhat problematic, as convention conditions resulted in predominant boronic acid hydrolysis and recovery of substantial 15, with only a small amount of 16 isolated (27% yield). Use of Pd$_2$(dba)$_3$ with PCy$_3$, however, gave 16 in acceptable yield (53%, 77% based on recovered starting material [brsm]), with recovery of 15 (31%). While most of the material was carried forward using this protocol, it was found

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<tbody>
<tr>
<td>10d</td>
<td>11a</td>
<td>12e (76)</td>
<td>13e (61)</td>
<td>8e (84)</td>
</tr>
<tr>
<td>10a</td>
<td>11c</td>
<td>12f (81)</td>
<td>13f (56)</td>
<td>8f (98)</td>
</tr>
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</table>

*Yields are in parentheses.*
ultimately that use of the PEPPSI-iPr catalyst enabled formation of 16 in 79% yield.\textsuperscript{19} Formation of 8h was accomplished from 16 in a straightforward manner (83% yield) with Co\textsubscript{2}(CO)\textsubscript{8}.

**Scheme 4. Preparation of 8h.**

With the Nicholas reaction precursors in hand, attention was turned to investigation of the cyclizations. Under conditions developed previously for benzocycloheptyne ring closure reactions, 8a (0.005 M in CH\textsubscript{2}Cl\textsubscript{2}) underwent reaction in the presence of BF\textsubscript{3}-OEt\textsubscript{2} (3 equiv), giving dibenzocycloheptyne 9a over 2.5 h (56% yield) (Table 2, entry 1). As a small amount of decomposition was evident chromatographically during this process, and with the belief that this could be due to the acid liberated during the substitution process, the reaction was conducted with the addition of 1.5 equiv. i-Pr\textsubscript{2}NEt. Although the reaction occurred somewhat more slowly (6 h) (entry 2), 9a could be isolated in improved yield (71%). These conditions (3 equiv. BF\textsubscript{3}-OEt\textsubscript{2}, 1.5 equiv. i-Pr\textsubscript{2}NEt, 0.005-0.01 M) were applied to 8b-8h (Table 2), and afforded fair to excellent yields of 9b-h. While there was some variation in required reaction time (4.5 – 16 h) and substrate, there was no particular correlation between reaction
time and substitution pattern of the arene behaving as nucleophile. In the case of trimethoxy substituted 8b, TLC analysis suggested the onset of some decomposition without complete conversion at 16 h, so that the reaction was terminated at this point and small amount of 8b (10%) could be recovered in addition to the isolated 9b (59% yield) (entry 3). 3-Thienyl substituted case 8d underwent competitive cyclization at C-2’ and C-4’, affording 9d and 9d’ and a regioisomeric mixture (82%, 45:55 9d:9d’) (entry 5). It is also worthy of note that 8c • 9c (entry 4) and 8g • 9g (entry 8) proceeded uneventfully, as the less electron rich arene nucleophiles would be of borderline reactivity and insufficient reactivity, respectively, for participation in intermolecular Nicholas reactions.\textsuperscript{15} Evidence of restricted rotation about the aryl-aryl bond was present for several of the cyclization products, as all dibenzocycloheptyne-Co\textsubscript{2}(CO)\textsubscript{6} complexes bearing an additional substituent ortho to the biaryl gave diastereotopic CH\textsubscript{2}’s for the propargylic hydrogen atoms in the \textsuperscript{1}H NMR spectra (9a, b, f, g). In addition, those bearing substitutents ortho to the cycloheptyne either gave a diastereotopic CH\textsubscript{2} (9c) or one right at coalescence (9h).

Table 2. Intramolecular Nicholas Reactions of 8.
8a-h → 9a-h

\[
\begin{array}{cccccc}
R^1 & R^2 & R^3 & R^4 & R^5 & R^6 \\
9a & OMe & H & OMe & OMe & OMe & H \\
b & H & H & OMe & OMe & OMe & H \\
c & OMe & H & H & Me & H & Me \\
e & OMe & H & H & OMe & OMe & OMe \\
f & OMe & OMe & OMe & OMe & OMe & H \\
g & H & H & H & H & H & H \\
h & CO_2Me & H & OMe & OMe & OMe & H \\
\end{array}
\]

9d

9d'

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<thead>
<tr>
<th>Entry</th>
<th>8</th>
<th>time</th>
<th>9</th>
<th>Yield (%)</th>
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<tr>
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<td>2.5 h</td>
<td>9a</td>
<td>56(^a)</td>
</tr>
<tr>
<td>2</td>
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<td>6 h</td>
<td>9a</td>
<td>71</td>
</tr>
<tr>
<td>3</td>
<td>8b</td>
<td>16 h</td>
<td>9b</td>
<td>59 (66)(^b)</td>
</tr>
<tr>
<td>4</td>
<td>8c</td>
<td>6 h</td>
<td>9c</td>
<td>85</td>
</tr>
<tr>
<td>5</td>
<td>8d</td>
<td>5 h</td>
<td>9d</td>
<td>82(^c)</td>
</tr>
<tr>
<td>6</td>
<td>8e</td>
<td>4.5 h</td>
<td>9e</td>
<td>91</td>
</tr>
<tr>
<td>7</td>
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<td>4.5 h</td>
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<td>16 h</td>
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</tr>
<tr>
<td>9</td>
<td>8h</td>
<td>5 h</td>
<td>9h</td>
<td>84</td>
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\(^a\) No i-Pr\(_2\)NEt added. \(^b\) Yields in parentheses based on
recovered starting material. \(^c\) Isolated as a 45:55 9d:9d’ mixture.
Removal of the Co$_2$(CO)$_6$ fragment for use in synthesis require concomitant conversion of the alkyne function into one compatible with the seven-membered ring.$^{20,21}$ The most commonly employed reagent for this purpose, Bu$_3$SnH, has caused some isomerization in related benzocycloheptyne cases;\textsuperscript{12c} consequently we chose to apply a modification of Isobe’s hydrosilylation protocol\textsuperscript{20} that would afford the alkene. Addition of triethyilsilane to the dibenzocycloheptyne complexes 9 in the presence of bis(trimethylsilylacetylene) (BTMSE) gave a regioisomeric mixture of silylated cycloheptenes, which were not isolated, but subjected to in situ desilylation with trifluoroacetic acid (TFA) to give the dibenzocycloheptenes 17. These dibenzocycloheptenes (17a,e,f,h) were isolated in good to excellent yields, and with no evidence of double bond isomerization during the reductive decomplexation process (Table 3).

**Table 3.** Conversion of 9 to dibenzocycloheptanones 18.
<table>
<thead>
<tr>
<th>9f</th>
<th>17f</th>
<th>90</th>
<th>18f</th>
<th>67</th>
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<tbody>
<tr>
<td>9h</td>
<td>17h</td>
<td>79</td>
<td>18h</td>
<td>81</td>
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"Oxidation under Swern conditions (oxalyl chloride-DMSO, Et₃N).

**Formal synthesis of (-)-allocolchicine.** Since several of the existing syntheses of allocolchicines employ the dibenzocycloheptanones (18) as critical intermediates, conversion of dibenzocycloheptenes 17 to 18 was considered to be the most prudent approach toward their synthesis. Hydroboration-oxidation of 17h with BH₃·THF/H₂O₂, with further oxidation of the intermediate alcohol using PDC, afforded ketone 18h in good yield (81%). Dibenzocycloheptanone 18h has been converted to (-)-allocolchine by Wulff, and as such this represents a formal synthesis of this natural product.

Similarly, treatment of 17f by BH₃·THF/H₂O₂ followed by oxidation with PDC afforded 18f (67% yield). Dibenzocycloheptanone 18f is a degradation product of (-)-androbiphenyline that has been prepared previously by Seitz, and found to be equally potent to (-)-androbiphenyline in inhibition of tubulin assembly.

**Synthesis of (-)-N-acetylcolchicine O-Methyl Ether (NSC 51046) and analog.** Conversion of 17a to ketone 18a was accomplished by hydroboration-oxidation with further oxidation under Swern conditions (DMSO-oxalyl chloride, Et₃N), giving the ketone in 80% yield. Adopting the approach of Wulff’s group towards (-)-allocolchicine, the reduction of ketone 18a using the LiBH₄/tartrate derived boronate ester (TARB-NO₂) protocol of Singaram gave alcohol 19a in excellent yield and enantioselectivity (96% yield, 95% ee) (Scheme 5). Substitution of azide for the alcohol function by way of zinc azide/diisopropyl azodicarboxylate (DIAD) afforded 20a (64%), while azide reduction (H₂, Lindlar catalyst) of 20a and acetylation gave NSC 51046 (2) in 88% (93% ee), which was spectroscopically identical to literature report. Recrystallization of 2 gave this compound in >99% ee. To our knowledge this is the first asymmetric synthesis of 2.

**Scheme 5.** Completion of Enantioselective Synthesis of NSC 51046 and its 3,8,9,10-tetramethoxy isomer.
Similarly, dibenzocycloheptene 17e was converted to an isomeric 3,8,9,10-tetramethoxyallocolchicine (21). Hydroboration-oxidation of 17e and further oxidation with PDC afforded dibenzocycloheptanone 18e in 68% yield. LiBH₄/TARB-NO₂ based reduction afforded the highly enantiomerically enriched alcohol 19e (98% yield, 98% ee) provided an extended period substrate/TARB-NO₂ mixing and slow LiBH₄ addition protocol was followed. Zinc azide based substitution of the alcohol afforded 20e without incident (77% yield), while reduction and acetylation gave 21 in 79% yield (95% ee); once again, a single recrystallization enriched this compound to >99% ee. To our knowledge, this is the first example of an allocolchicine with an 8,9,10-oxygenated A ring.

In summary, intramolecular Nicholas reactions have proven to be effective in the synthesis of dibenzocycloheptyne-Co₂(CO)₆ complexes. Ready decomplexation to the dibenzocycloheptenes allows application of this methodology to the synthesis of allocolchicines or their derivatives, including tubulin-inhibiting ketone 6,7-dihydro-3,4,9,10,11-pentamethoxy-5H-Dibenzo[a,c]cyclohepten-5-one (18f), a formal total synthesis of (-)-allocolchicine (1), the enantioselective total synthesis of N-acetylallocolchinol O-methyl ether (NSC 51046, 2), and of the 3,8,9,10-tetramethoxy isomer of NSC 51046 (21).

Experimental Section
**General Methods:** All reaction solvents were used after passage through a solvent purification system. Commercial BF$_3$-OEt$_2$ was distilled and stored under nitrogen. All reactions were conducted under a nitrogen atmosphere unless otherwise noted. Flash chromatography was performed as described by Still using silica gel 60 (230-400 mesh). 2-Bromo-5-methoxybenzaldehyde$^{27}$ and 6-bromo-2,3-dimethoxybenzaldehyde$^{28}$ were prepared by literature methods and are >95% purity as determined by $^1$H and $^{13}$C NMR spectroscopy. All new compounds are >95% purity as determined by $^1$H and $^{13}$C NMR spectroscopy. NMR spectra were run at 500 MHz or 300 MHz for $^1$H and 125 MHz or 75 MHz for $^{13}$C in CDCl$_3$; chemical shifts are given in ppm and coupling constants ($J$) are given in Hz. High resolution mass spectra were run by time of flight mass spectroscopy, in EI mode, at 70 eV.

2',3',4,4'-Tetramethoxy[1,1'-Biphenyl]-2-carboxaldehyde (12a). Prepared according to the method of Fürstner,$^{17}$ 11a (0.3517 g, 1.16 mmol), afforded 7a (0.4202 g, 85%); mp 102-3 °C (hexanes); lit.$^{17}$ 102-3 °C. This compound >95% purity as determined by $^1$H and $^{13}$C NMR spectroscopy.

2',3',4'-Trimethoxy[1,1'-Biphenyl]-2-carboxaldehyde (12b). Prepared according to the method of Fürstner,$^{17}$ 11b (0.2278 g, 1.23 mmol), affording 12b (0.3706 g, 92%); mp 105-5.5 °C (hexanes); lit.$^{17}$ 98-99 °C. This compound >95% purity as determined by $^1$H and $^{13}$C NMR spectroscopy.

4-Methoxy-3',5'-dimethyl[1,1'-biphenyl]-2-carboxaldehyde (12c). Prepared as adapted from the method of Fürstner,$^{17}$ employing 11a (0.9593 g, 4.46 mmol) and (3,5-dimethylphenyl)boronic acid (6b) (1.3423 g, 8.96 mmol) to give 12c (0.8472 g, 79% yield), following flash chromatographic purification (15:1 petroleum ether : Et$_2$O), as a colorless viscous oil which solidified upon standing; mp 71-2 °C; IR (KBr) $\nu_{\text{max}}$ 3006, 2917, 1688, 1604 cm$^{-1}$; $^1$H NMR 9.97 (s, 1H), 7.52 (d, $J = 2.8$, 1H), 7.37 (d, $J = 8.5$, 1H), 7.19 (dd, $J = 8.5$, 2.8, 1H), 7.06 (br s, 1H), 6.97 (br s, 2H), 3.90 (s, 3H), 2.39 (s, 6H); $^{13}$C NMR 192.4, 159.0, 139.4, 137.9, 137.4, 134.5, 131.9, 129.3, 128.1, 121.2, 109.7, 55.5, 21.2; MS m/e 240 (M$^+$); HRMS m/e for C$_{16}$H$_{16}$O$_2$ calcd. 240.1150 (M$^+$), found 240.1140.

5-Methoxy-2-(3-thienyl)benzaldehyde (12d). Prepared as adapted from the method of Fürstner,$^{17}$ employing 11a (0.2301 g, 1.07 mmol) and 3-thienylboronic acid (10c) (0.2003 g, 1.56 mmol) to give 12d (0.1900 g, 81% yield) following flash chromatographic purification (15:1 petroleum ether : Et$_2$O),
mp 68-69 °C (CH₂Cl₂); IR (KBr) \( \nu_{\text{max}} \) 3100, 2845, 1684 cm\(^{-1}\); \(^1\)H NMR \( \delta \) 10.08 (s, 1H), 7.50 (d, \( J = 2.7, 1H \)), 7.44 (dd, \( J = 4.8, 3.0, 1H \)), 7.41 (d, \( J = 8.5, 1H \)), 7.24 (dd, \( J = 3.0, 0.9, 1H \)), 7.19 (dd, \( J = 8.5, 2.7, 1H \)), 7.17 (dd, \( J = 4.8, 0.9, 1H \)), 3.90 (s, 3H); \(^{13}\)C NMR 192.2, 159.0, 137.9, 134.7, 133.5, 131.8, 129.4, 126.1, 124.5, 121.5, 109.7, 55.5; MS m/e 218 (M\(^+\)); HRMS m/e for C\(_{12}\)H\(_{10}\)O\(_2\)S calcd. 218.0402 (M\(^+\)), found 218.0399.

3',4,4',5'-Tetramethoxy[1,1'-biphenyl]-2-carboxaldehyde (12e). Prepared according to the method of Fürstner\(^{17}\) employing 11a (0.7000 g, 3.26 mmol) and 3,4,5-trimethoxyphenylboronic acid (10d) (1.0877 g, 4.89 mmol) to give 12e (0.7472 g, 76% yield) following flash chromatographic purification (3:1 petroleum ether : Et\(_2\)O), as a colorless solid, mp 134-136 °C; IR (KBr) 2931, 1687, 1604 cm\(^{-1}\); \(^1\)H NMR \( \delta \) 9.96 (s, 1H), 7.47 (d, \( J = 2.8, 1H \)), 7.37 (d, \( J = 8.5, 1H \)), 7.17 (dd, \( J = 8.5, 2.8, 1H \)), 6.52 (s, 2H), 3.89 (s, 3H), 3.88 (s, 3H), 3.87 (s, 6H); \(^{13}\)C NMR 192.2, 159.1, 152.9, 139.0, 137.7, 134.5, 133.1, 131.7, 121.2, 109.8, 107.5, 60.9, 56.2, 55.5; MS m/e (M\(^+\)) 302; HRMS m/e for C\(_{17}\)H\(_{18}\)O\(_5\) calcd. 302.1154, found 302.1139.

2',3,3',4,4'-Pentamethoxy[1,1'-Biphenyl]-2-carboxaldehyde (12f). Prepared according to the method of Fürstner\(^{17}\) employing 11c (0.7937 g, 3.24 mmol) and 2,3,4-trimethoxyphenylboronic acid (10a) (1.0993 g, 5.18 mmol) to give 12f (0.8712 g, 81% yield) following flash chromatographic purification (4:1 petroleum ether : EtOAc), mp 117-119 °C; IR (KBr) \( \nu_{\text{max}} \) 2938, 1699, 1593 cm\(^{-1}\); \(^1\)H NMR \( \delta \) 10.15 (s, 1H), 7.12 (d, \( J = 8.4, 1H \)), 7.01 (d, \( J = 8.4, 1H \)), 6.87 (d, \( J = 8.5, 1H \)), 6.71 (d, \( J = 8.5, 1H \)), 3.96 (s, 3H), 3.93 (s, 3H), 3.890 (s, 3H), 3.887 (s, 3H), 3.58 (s, 3H); \(^{13}\)C NMR 191.1, 153.2, 152.0, 150.5, 149.9, 141.7, 131.7, 129.0, 126.6, 125.7, 124.5, 115.9, 106.9, 61.7, 60.7, 60.3, 55.7, 55.7; MS m/e 332 (M\(^+\)); HRMS for C\(_{18}\)H\(_{20}\)O\(_6\) (M\(^+\)) calcd. 332.1260, found 332.1275.

3-(2',3',4,4'-Tetramethoxybiphenyl-2-yl)-2-propyn-1-ol (13a). General Procedure A. To a solution of 12a (0.3378 g, 1.12 mmol) in CH₂Cl₂ (10 mL) was added CBr\(_4\) (0.556 g, 1.68 mmol) and PPh\(_3\) (1.172 g, 4.47 mmol). After stirring for 4 h, petroleum ether (10 mL) and iodomethane (0.4 mL) were added, and the mixture allowed to stir for 8 h). The volatiles were removed under reduced pressure, and the residue filtered through silica gel, using 1:1 petroleum ether : Et\(_2\)O as solvent). The
filtrate was concentrated under reduced pressure to give the crude dibromide, which was used without further purification. The dibromide was dissolved in THF (20 mL), and cooled to -78 °C. Butyllithium (1.08 mL of a 2.58 M solution in hexanes, 2.79 mmol) was added, and stirring continued for 5 h. A suspension of paraformaldehyde (0.4 g, excess) in THF (5 mL) was added, and the reaction stirred for 8 h as the mixture gradually warmed to room temperature. A conventional extractive workup followed by flash chromatography (1:2 petroleum ether : Et₂O) gave 13a (0.2919 g, 80%), as a viscous oil; IR (KBr) \( \nu_{\text{max}} \) 3455 br, 2937, 2229 cm\(^{-1}\); \(^1\)H NMR \( \delta \) 7.22 (d, J = 8.6, 1H), 7.05 (d, J = 2.7, 1H), 6.28 (d, J = 8.5, 1H), 6.86 (dd, J = 8.8, 1H), 6.89 (dd, J = 8.8, 1H), 4.29 (s, 2H), 3.90 (s, 3H), 3.82 (s, 3H), 3.61 (s, 3H), 2.30 (br, 1H); \(^{13}\)C NMR 158.2, 153.1, 151.6, 142.0, 133.3, 131.3, 127.1, 125.6, 123.2, 116.8, 114.8, 106.7, 89.6, 85.2, 61.0, 60.9, 55.9, 55.3, 51.4; MS m/e 328 (M\(^+\)); HRMS m/e for C\(_{19}\)H\(_{20}\)O\(_5\) calcd. 328.1311 (M\(^+\)), found 328.1311.

3-(2',3',4'-Trimethoxybiphenyl-2-yl)-2-propyn-1-ol (13b). Reaction of aldehyde 12b (0.1514 g, 0.554 mmol) according to General Procedure A, afforded 13b (0.1293 g, 78% yield) following preparative TLC (1:2 hexanes : EtO\(_2\)), as a viscous oil; IR (KBr) \( \nu_{\text{max}} \) 3379 br, 2933, 2227 cm\(^{-1}\); \(^1\)H NMR \( \delta \) 7.52 (dd, J = 7.7, 1.0, 1H), 7.25-7.37 (m, 3H), 6.98 (d, J = 8.5, 1H), 6.71 (d, J = 8.6, 1H), 4.29 (s, 2H), 3.91 (s, 3H), 3.91 (s, 3H), 3.63 (s, 3H), 2.07 (br, 1H); \(^{13}\)C NMR 153.3, 151.5, 142.0, 140.8, 132.3, 130.2, 128.0, 127.5, 126.9, 125.3, 122.4, 106.8, 89.9, 85.2, 61.0, 60.9, 56.0, 51.4; MS m/e 298 (M\(^+\)); HRMS m/e for C\(_{18}\)H\(_{18}\)O\(_4\) calcd. 298.1205 (M\(^+\)), found 298.1201.

(3-Methoxy-3',5'-dimethylbiphenyl-2-yl)-2-propyn-1-ol (13c). Reaction of aldehyde 12c (0.8472 g, 3.53 mmol) according to General Procedure A, afforded 13c (0.5389 g, 57% yield) following flash chromatography (2:1 petroleum ether : EtO\(_2\)) as a viscous oil; IR (KBr) \( \nu_{\text{max}} \) 3400 br, 2917, 1603 cm\(^{-1}\); \(^1\)H NMR \( \delta \) 7.31 (d, J = 8.5, 1H), 7.20 (s, 2H), 7.08 (d, J = 2.8, 1H), 6.96 (dd, J = 8.5, 2.7, 1H), 4.37 (s, 2H), 3.84 (s, 3H), 2.38 (s, 6H), 1.55 (br, 1H); \(^{13}\)C NMR 158.3, 140.0, 137.3, 136.9, 130.6, 128.7, 127.1, 121.6, 117.4, 115.4, 89.8, 85.6, 55.4, 51.6, 21.3; MS m/e 266 (M\(^+\)); HRMS m/e for C\(_{18}\)H\(_{18}\)O\(_2\) calcd. 266.1307 (M\(^+\)), found 266.1294.
3-(5-Methoxy-2-(3-thienyl)phenyl)-2-propyn-1-ol (13d) and 7-methoxynaphtho[2,1-b]thiophene (14). Reaction of aldehyde 12d (0.0876 g, 0.401 mmol) according to General Procedure A gave, in order of elution, 14 (0.0452 g, 53% yield) and 13d (0.0389 g, 40% yield), following preparative TLC (1:1 petroleum ether : Et₂O); 14 as a colorless solid, mp 118-120 °C; IR (KBr) \( \nu_{\text{max}} \) 2956, 1621 cm⁻¹; \(^1\)H NMR \( \delta \) 8.26 (d, \( J = 8.8 \), 1H), 7.92 (d, \( J = 5.4 \), 1H), 7.87 (d, \( J = 8.7 \), 1H), 7.67 (d, \( J = 8.7 \), 1H), 7.58 (d, \( J = 5.4 \), 1H), 72.6-7.31 (m, 2H), 3.97 (s, 3H); \(^13\)C NMR 157.2, 136.1, 135.4, 132.2, 125.9, 125.1, 124.5, 124.3, 121.7, 121.2, 118.0, 107.6, 55.4; MS m/e 214 (M⁺); HRMS for C\(_{13}\)H\(_{10}\)O\(_2\)S (M⁺) calcd. 214.0452, found 214.0454. 13d as a viscous oil; IR (KBr) \( \nu_{\text{max}} \) 3384 br, 2928, 2228 cm⁻¹; \(^1\)H NMR \( \delta \) 7.54 (dd, \( J = 3.0 \), 1.4, 1H), 7.42 (dd, \( J = 5.0 \), 1.4, 1H), 7.34 (d, \( J = 8.6 \), 1H), 7.34 (dd, \( J = 5.0 \), 3.0, 1H), 7.06 (d, \( J = 2.7 \), 1H), 6.93 (dd, \( J = 8.6 \), 2.7H) 4.46 (d, \( J = 4.2 \), 2H), 3.84 (s, 3H), 1.61 (br, 1H); \(^13\)C NMR 158.2, 140.5, 131.2, 130.2, 128.5, 124.7, 122.6, 121.2, 117.7, 115.6, 90.2, 85.7, 55.4, 51.8; MS m/e 244 (M⁺); HRMS m/e for C\(_{14}\)H\(_{12}\)O\(_2\)S calcd. 244.0558 (M⁺), found 244.0550.

3-(3',4,4',5'-Tetramethoxybiphenyl-2-yl)-2-propyn-1-ol (13e). Reaction of aldehyde 12e (0.4674 g, 1.55 mmol) according to General Procedure A, gave 13e (0.3115 g, 61% yield), following flash chromatography (1:1 petroleum ether : Et₂O), as a viscous oil; IR (KBr) 3500 (br), 2935, 2224, 1602 cm⁻¹; \(^1\)H NMR \( \delta \) 7.29 (d, \( J = 8.6 \), 1H), 7.06 (d, \( J = 2.7 \), 1H), 6.92 (dd, \( J = 8.6 \), 2.7, 1H), 6.79 (s, 2H), 4.38 (s, 2H), 3.88 (s, 3H), 3.87 (s, 6H), 3.81 (s, 3H), 2.33 (br s, 1H); \(^13\)C NMR 158.2, 152.5, 137.0, 136.1, 135.4, 130.3, 121.3, 117.6, 115.2, 106.4, 90.3, 84.8, 60.7, 56.0, 55.2, 51.2; MS m/e (M⁺) 328; HRMS m/e for C\(_{19}\)H\(_{20}\)O\(_5\) calcd. 328.1311, found 328.1308.

3-(2',3',3',4,4'-Pentamethoxybiphenyl-2-yl)-2-propyn-1-ol (13f). Reaction of aldehyde 12f (0.8629 g, 2.60 mmol) according to General Procedure A, gave 13f (0.5257 g, 56% yield), flash chromatography (1:1 hexanes : Et₂O), as a viscous oil; IR (KBr) 3509 (br), 2936, 2227, 1591 cm⁻¹; \(^1\)H NMR \( \delta \) 6.96 (d, \( J = 8.5 \), 1H), 6.91 (d, \( J = 8.6 \), 1H), 6.88 (d, \( J = 8.5 \), 1H), 6.64 (d, \( J = 8.6 \), 1H), 4.28 (br d, \( J = 4.8 \), 2H), 3.89 (s, 3H), 3.85 (s, 3H), 3.84 (s, 3H), 3.83 (s, 3H), 2.88 (br, 1H); \(^13\)C NMR 152.8, 151.24, 151.17, 149.9, 141.6, 133.9, 126.7, 125.4, 125.3, 117.4, 112.0, 106.4, 94.3, 80.3, 60.7, 60.61, 60.57, 55.6, 51.0; MS m/e 358 (M⁺); HRMS m/e for C\(_{20}\)H\(_{20}\)O\(_6\) calcd. 358.1416, found 358.1404.
3-Biphenyl-2-yl-2-propyn-1-ol (13g). To a solution of 2′-iodobiphenyl (0.10 mL, 0.57 mmol), Pd(PPh₃)₄ (10 mg) and CuI (20 mg) in degassed diisopropylamine (5 mL) was added propargyl alcohol (0.15 mL, 2.6 mmol). After 20 h of stirring, the volatiles were removed under reduced pressure, the residue was filtered through silica with Et₂O, and the volatiles again removed in vacuo. Preparative TLC in 2:1 hexanes:Et₂O gave 0.1025 g of 13g (87% yield), bp 135-140 °C (0.15 torr) (bulb-to-bulb); IR (KBr) νₐ₅ 3054, 3061, 2925, 2235 cm⁻¹; ¹H NMR 7.58 (d, J = 7.3, 2H), 7.57 (d, J = 7.9, 1H), 7.44 (apparent t, Javs = 7.5, 2H), 7.35-7.41 (m, 3H), 7.31 (m, 1H), 4.35 (s, 2H), 1.63 (br s, 1H); ¹³C NMR (40 °C) 144.0, 140.5, 133.1, 129.5, 129.2, 128.6, 127.9, 127.4, 127.0, 121.0, 90.2, 85.4, 51.5; MS m/e 208 (M⁺); HRMS m/e for C₁₅H₁₂O calcd. 208.0888 (M⁺), found 208.0890.

Methyl 4-bromo-3-iodobenzoate. To a solution of 4-bromo-3-iodobenzoic acid (1.3227 g, 3.68 mmol) in methanol (40 mL) was added H₂SO₄ (10 drops). The mixture was heated to reflux for 12 h. Following a conventional extractive workup (Et₂O), and extraction of the Et₂O layers with NaOH (aq), the Et₂O layers were dried over MgSO₄, filtered and concentrated under reduced pressure. Flash chromatography (8:1 petroleum ether:Et₂O) afforded methyl 4-bromo-3-iodobenzoate (1.2550 g, 91% yield) as a colorless solid, mp 70-71 °C; IR (KBr) νₐ₅ 3087, 1726 cm⁻¹; ¹H NMR 8.46 (s, 1H), 7.81 (d, J = 8.2, 1H), 3.90 (s, 3H); ¹³C NMR 164.8, 141.1, 135.2, 130.12, 130.08, 101.0, 52.5; MS m/e (M⁺) 340/342; HRMS m/e for C₈H₆BrIO₂ calcd. 339.8596, found 339.8603.

Methyl 4-bromo-3-(3-methoxyprop-1-ynyl)benzoate (15). To a solution of methyl 4-bromo-3-iodobenzoate (1.255 g, 3.21 mmol) and propargyl methyl ether (0.47 mL, 5.9 mmol) in diisopropylamine (5 mL) was added CuI (0.0404 g, 0.212 mmol) and Pd(PPh₃)₄ (0.070 g, 0.061 mmol). After stirring 12 h, the mixture was subjected to a conventional extractive workup. Flash chromatography (5:1 petroleum ether:Et₂O) afforded 15 (0.9599 g, 92% yield) as yellow crystals, mp 42-43 °C; IR (KBr) νₐ₅ 3033, 2953, 1739, 1593 cm⁻¹; ¹H NMR 8.10 (d, J = 2.0, 1H), 7.78 (dd, J = 8.4, 2.0, 1H), 7.64 (d, J = 8.4, 1H), 4.37 (s, 2H), 3.89 (s, 3H), 3.48 (s, 3H); ¹³C NMR 165.6, 134.4, 132.5, 130.6, 130.1, 129.2, 125.2, 90.7, 84.0, 60.2, 57.7, 52.3; MS m/e 282/284 (M⁺); HRMS for C₁₂H₁₁BrO₃ calcd. 283.9891, found 283.9900.
Methyl 2',3',4'-trimethoxy-2-(3-methoxyprop-1-ynyl)biphenyl-4-carboxylate (16). A mixture of methyl 4-bromo-3-(3-methoxyprop-1-ynyl)benzoate (15) (0.0712 g, 0.251 mmol), 2,3,4-trimethoxyphenylboronic acid (10a) (0.1333 g, 0.629 mmol), K$_3$PO$_4$ (0.1590 g, 0.750 mmol), Pd$_2$(dba)$_3$ (0.0046 g, 0.0050 mmol), PCy$_3$ (0.0035 g, 0.012 mmol) in toluene (10 mL) was heated to 100 °C for 37 h. Following an extractive workup, radial chromatography (5:1 petroleum ether:Et$_2$O) afforded, in order of elution, recovered 15 (0.0218 g, 31% recovery), and 16 (0.0493 g, 53% yield) as a viscous oil; IR (KBr) $\nu_{\text{max}}$ 2936, 1730, 1605 cm$^{-1}$; $^1$H NMR $\delta$ 8.22 (d, J = 1.8, 1H), 8.00 (dd, J = 8.1, 1.8, 1H), 7.41 (d, J = 8.1, 1H), 7.01 (d, J = 8.5, 1H), 6.72 (d, J = 8.5, 1H), 4.20 (s, 2H), 3.94 (s, 3H), 3.92 (s, 3H), 3.91 (s, 3H), 3.66 (s, 3H), 3.23 (s, 3H); $^{13}$C NMR 166.4, 153.8, 151.4, 145.3, 142.1, 133.7, 130.6, 128.9, 126.6, 125.2, 122.9, 106.7, 88.2, 85.2, 61.2, 61.0, 60.2, 57.2, 56.1, 52.2; MS m/e 370 (M$^+$); HRMS for C$_{21}$H$_{22}$O$_6$(M$^+$) calcd. 370.1416, found 370.1416.

A solution of potassium tert-butoxide (0.0351 g, 0.314 mmol) and (1,3-diisopropylimiazol-2-ylidene)(3-chloropyridyl)palladium(II) dichloride (0.0014 g, 1 mol%) is isopropanol (1 mL) was stirred for 10 min. To this solution was added 2,3,4-trimethoxyphenylboronic acid (10a) (0.0975 g, 0.460 mmol) and 15 (0.0590 g, 0.209 mmol). After stirring for 12 h, diethyl ether was added and reaction subjected to a conventional extractive workup (Et$_2$O). Preparative TLC (5:1 petroleum ether:Et$_2$O) afforded 16 (0.0612 g, 79% yield).

Hexacarbonyl[µ-$^4$-(3-acetoxy-(2',3',4,4'-tetramethoxybiphenyl-2-yl)-1-propyne)]dicobalt (8a). General Procedure B. To alcohol 13a (0.2875 g, 0.876 mmol) at 0 °C was added acetic anhydride (1 mL) and pyridine (1 mL). The solution was stirred 4h, as the solution came to room temperature. The volatiles were removed under reduced pressure, and the residue dissolved in CH$_2$Cl$_2$ (25 mL). An unweighed amount of octacarbonyldicobalt (excess) was added and the mixture stirred 4h. After concentration under reduced pressure, flash chromatography (100% petroleum ether – 5:1 petroleum ether : Et$_2$O) gave acetate complex 8a (0.4952 g, 86% yield) as a red-brown solid, mp 122-124 °C; IR (KBr) $\nu_{\text{max}}$ 2919, 2090, 2050, 2018, 1743 cm$^{-1}$; $^1$H NMR $\delta$ 7.30 (d, J = 2.5, 1H), 7.00 (d, J = 8.5, 1H), 6.88 (dd, J = 8.5, 2.5, 1H), 6.80 (d, J = 8.5, 1H), 6.73 (d, J = 8.5, 1H), 4.58 (d, J = 15.0, 1H), 3.97 (d, J =
15.0, 1H), 3.96 (s, 3H), 3.93 (s, 3H), 3.86 (s, 3H), 3.59 (s, 3H), 2.02 (s, 3H); $^{13}$C NMR 199.4, 199.3, 170.3, 159.2, 153.9, 151.2, 142.4, 137.6, 131.8, 129.4, 128.2, 125.4, 118.0, 114.5, 107.3, 92.5, 88.7, 64.4, 60.7, 60.4, 56.2, 55.0, 20.2; MS m/e 600 (M$^+$-2CO), 572 (M$^+$-3CO), 488 (M$^+$-6CO); Anal. Calcd. for C$_{27}$H$_{22}$Co$_2$O$_{12}$ C, 49.41; H, 3.38. Found C, 49.68; H, 3.38.

Hexacarbonyl[$\mu^{-}$(3-acetoxy-(2',3',4'-trimethoxybiphenyl-2-yl)-1-propyne)dicobalt] (8b).

Subjecting 13b (0.2140 g, 0.407 mmol) to General Procedure B afforded 18b (0.2140 g, 84% yield) following flash chromatographic purification (10:1 – 4:1 petroleum ether:Et$_2$O), as a red-brown solid, mp 108-110 °C; IR (KBr) $\nu_{\text{max}}$ 2938, 2090, 2052, 2022, 1745 cm$^{-1}$; $^{1}$H NMR $\delta$ 7.76 (d, J = 7.8, 1H), 7.40 (apparent t, J = 7.4, 1H), 7.31 (apparent t, J = 7.3, 1H), 7.11 (d, J = 7.5, 1H), 6.82 (d, J = 8.4, 1H), 6.75 (d, J = 8.4, 1H), 4.59 (d, J = 14.5, 1H), 3.98 (d, J = 14.5, 1H), 3.98 (s, 3H), 3.94 (s, 3H), 3.60 (s, 3H), 2.03 (s, 3H); $^{13}$C NMR 199.3, 170.4, 154.1, 151.5, 142.6, 137.1, 136.6, 134.3, 130.9, 128.6, 128.1, 127.4, 125.0, 107.5, 92.6, 88.6, 64.6, 60.8, 60.5, 56.4. 20.2; MS m/e 570 (M$^+$-2CO), 542 (M$^+$-3CO), 458 (M$^+$-6CO); HRMS m/e for C$_{26}$H$_{20}$Co$_2$O$_{11}$ calcd. 597.9720 (M$^+$-CO), found 597.9741.

Hexacarbonyl[$\mu^{-}$(3-acetoxy-(3-methoxy-3',5'-dimethylbiphenyl-2-yl)-1-propyne)dicobalt] (8c).

Subjecting 13c (0.0608 g, 0.228 mmol) to General Procedure B afforded acetate complex 8c (0.1232 g, 91% yield) following flash chromatography (10:1 petroleum ether : Et$_2$O), as a red-brown solid, mp 250 °C (dec.); IR (KBr) $\nu_{\text{max}}$ 2961, 2090, 2058, 1998, 1748 cm$^{-1}$; $^{1}$H NMR $\delta$ 7.28 (d, J = 2.7, 1H), 7.08 (s, 1H), 7.04 (d, J = 8.4, 1H), 6.89 (dd, J = 8.4, 2.7, 1H), 6.86 (s, 2H), 4.02 (s, 2H), 3.87 (s, 3H), 2.37 (s, 6H), 2.04 (s, 3H); $^{13}$C NMR 199.4, 170.4, 159.2, 141.6, 138.2, 136.4, 134.2, 131.1, 129.2, 127.4, 118.0, 114.6, 93.3, 88.9, 64.2, 55.2, 21.1, 20.3; MS m/e 566 (M$^+$-CO), 510 (M$^+$-3CO), 426 (M$^+$-6CO); HRMS m/e for C$_{26}$H$_{20}$Co$_2$O$_{9}$ calcd. 565.9822 (M$^+$-CO), found 565.9811.

Hexacarbonyl[$\mu^{-}$(3-Acetoxy-1-(5-methoxy-2-(3-thienyl)phenyl-1-propyne)dicobalt] (8d).

Subjecting 13d (0.0418 g, 0.171 mmol) to General Procedure B gave acetate complex 8d (0.0756, 77% yield) following flash chromatography (10:1 petroleum ether : Et$_2$O), as a red-brown solid, mp 104-105 °C; IR (KBr) $\nu_{\text{max}}$ 2941, 2090, 2055, 2021, 1745 cm$^{-1}$; $^{1}$H NMR $\delta$ 7.46 (dd, J = 4.7, 3.1, 1H), 7.28 (d, J = 2.6, 1H), 7.15 (m, 1H), 7.06 (d, J = 8.4, 1H), 7.02 (d, J = 4.7, 1H), 6.88 (dd, J = 8.4, 2.6, 1H), 4.30 (s,
Hexacarbonyl[mu-\eta^4-(3-acetoxy-(3',4,4',5'-tetramethoxybiphenyl-2-yl)-1-propyne)]dicobalt (8e).

Subjecting 13e (0.2809 g, 0.855 mmol) to General Procedure B afforded 8e (0.4722 g, 84% yield) following flash chromatographic purification (3:1 petroleum ether : Et_2O), as a red-brown solid; mp 126-128 °C; IR (KBr) \(\nu_{\text{max}}\) 2938, 2090, 2010, 1974, 1748 cm\(^{-1}\); \(^1\)H NMR \(\delta\) 7.27 (d, J = 2.6, 1H), 7.05 (d, J = 8.4, 1H), 6.89 (dd, J = 8.4, 2.6, 1H), 6.42 (s, 2H), 4.22 (s, 2H), 3.93 (s, 3H), 3.86 (s, 3H), 3.82 (s, 6H), 2.02 (s, 3H); \(^{13}\)C NMR 199.3, 170.3, 159.4, 153.2, 137.7, 137.3, 136.4, 133.6, 131.2, 117.7, 114.7, 106.9, 93.1, 88.3, 63.9, 61.1, 56.1, 55.1, 20.2; MS m/e 628 (M\(^+-\)CO), 600 (M\(^+-\)2CO), 572 (M\(^+-\)3CO), 544 (M\(^+-\)4CO), 516 (M\(^+-\)5CO), 488 (M\(^+-\)6CO); HRMS for C\(_{27}\)H\(_{22}\)Co\(_2\)O\(_{12}\) calcd (M\(^+-\)CO) 627.9826, found 627.9802.

Hexacarbonyl[mu-\eta^4-(3-acetoxy-(2',3,3',4,4'-pentamethoxybiphenyl-2-yl)-1-propyne)]dicobalt (8f).

Subjecting 13f (0.5231 g, 1.46 mmol) to General Procedure B afforded 8f (0.9818 g, 98% yield) following flash chromatographic purification (4:1 petroleum ether : Et_2O), as a red-brown solid, mp 120-121 °C; IR (KBr) \(\nu_{\text{max}}\) 3002, 2939, 2088, 2090, 1743 cm\(^{-1}\); \(^1\)H NMR \(\delta\) 6.95 (d, J = 8.4, 1H), 6.80 (d, J = 8.4, 1H), 6.73 (d, J = 8.4, 1H), 6.71 (d, J = 8.4, 1H), 4.53 (d, J = 14.5, 1H), 4.07 (s, 3H), 3.95 (s, 3H), 3.92 (s, 3H), 3.90 (s, 3H), 3.83 (d, J = 14.5, 1H), 3.61 (s, 3H), 2.00 (s, 3H); \(^{13}\)C NMR 199.8, 170.4, 153.9, 151.6, 151.4, 149.5, 142.4, 131.3, 128.84, 128.79, 125.6, 125.4, 112.2, 107.2, 94.3, 81.0, 65.4, 60.6, 60.3, 59.9, 56.2, 55.7, 20.2; MS m/e 630 (M\(^+-\)2CO), 602 (M\(^+-\)3CO), 518 (M\(^+-\)5CO), 400 (M\(^+-\)Co_2(CO)_6); HRMS for C\(_{28}\)H\(_{24}\)Co_2O\(_{13}\) (M\(^+-\)2CO) calcd. 629.9997, found 629.9995.

Hexacarbonyl[mu-\eta^4-(3-Acetoxy-1-biphenyl-2-yl)-1-propyne]dicobalt (8g).

Subjecting 13g (0.0799 g, 0.384 mmol) to General Procedure B gave acetate complex 8g (0.1763 g, 86% yield) following flash chromatography (50:1 petroleum ether : Et_2O), as a red-brown oil which gradually solidified, mp 99-101 °C; IR (KBr) \(\nu_{\text{max}}\) 3073, 2977, 2087, 2055, 2006, 1749 cm\(^{-1}\); \(^1\)H NMR \(\delta\) 7.77 (d, J = 7.8, 1H), 7.45-7.52 (m, 3H), 7.42 (apparent t, J\(_{\text{ave}}\) = 7.6, 1H), 7.34 (apparent t, J\(_{\text{ave}}\) = 7.3, 1H), 7.26-7.30 (m, 2H), 7.14 (d, J =
7.8, 1H), 4.02 (s, 2H), 2.02 (s, 3H); $^{13}$C NMR 199.3, 170.4, 142.2, 141.2, 135.3, 134.3, 130.2, 129.3, 128.6, 128.3, 128.0, 127.6, 93.1, 88.4, 64.1, 20.3; MS m/e 480 (M$^+$-2CO), 452 (M$^+$-3CO), 396 (M$^+$-5CO), 368 (M$^+$-6CO); Anal. Calcd. for C$_{23}$H$_{14}$Co$_2$O$_8$. C, 51.52; H, 2.63. Found C, 51.75; H, 2.51.

Hexacarbonyl[$\mu^{-4}$-(3-methoxy-(4-carbomethoxy-2',3',4'-trimethoxybiphenyl-2-yl)-1-propyne)]dicobalt (8h). To a solution of 16 (0.1223 g, 0.330 mmol) in CH$_2$Cl$_2$ at 0 °C was added octacarbonyldicobalt (excess). The cooling bath was removed and the mixture allowed to stir for 2h. After concentration under reduced pressure, flash chromatography (3:1 petroleum ether : Et$_2$O) afforded 8h (0.1797 g, 83% yield) as a red-brown solid, mp 143-144 °C; IR (KBr) $\nu$ max 2956, 2091, 2039, 2009, 1726 cm$^{-1}$; $^1$H NMR 8.45 (d, J = 1.7, 1H), 7.93 (dd, J = 7.9, 1.7, 1H), 7.18 (d, J = 7.9, 1H), 6.80 (1/2 AB quartet, J = 8.5, 1H), 6.74 (1/2 AB quartet, J = 8.5, 1H), 3.97 (s, 3H), 3.96 (s, 3H), 3.94 (s, 3H), 3.87 (d, J = 13.4, 1H), 3.59 (s, 3H), 3.30 (s, 3H), 3.25 (d, J = 13.4, 1H); $^{13}$C NMR 199.4, 166.6, 154.0, 151.3, 142.4, 141.3, 137.8, 135.7, 131.2, 130.1, 128.1, 127.8, 124.9, 107.1, 95.7, 86.0, 71.7, 60.8, 60.6, 58.6, 56.3, 52.3; MS m/e 572 (M$^+$-3CO), 516 (M$^+$-5CO); HRMS for C$_{27}$H$_{22}$Co$_2$O$_{12}$ calcd (M$^+$-3CO) 571.9928, found 571.9924.

Hexacarbonyl[$\mu^{-4}$-(1,2,3,9-tetramethoxy-5H-dibenzo[a,c]cycloheptyne)]dicobalt (9a). General Procedure C. To a solution of 8a (0.1193 g, 0.182 mmol) in CH$_2$Cl$_2$ (35 mL) at 0 °C was added diisopropylethylamine (48 $\mu$L, 1.5 equiv) and BF$_3$-OEt$_2$ (69 $\mu$L, 3.0 equiv). The cooling bath was removed and the reaction allowed to stir for 6h, at which time consumption of starting material was complete. Following an extractive workup, flash chromatography (5:1 petroleum ether : Et$_2$O) afforded 9a (0.0766 g, 71% yield), as a red-brown oil which gradually solidified, mp 117-119 °C; IR (KBr) $\nu$ max cm$^{-1}$; $^1$H NMR 7.57 (d, J = 8.5, 1H), 7.21 (d, J = 3.0, 1H), 6.92 (dd, J = 8.5, 2.5, 1H), 6.65 (s, 1H), 4.01 (d, J = 14.0, 1H), 3.91 (s, 3H), 3.90 (s, 3H), 3.82 (s, 3H), 3.63 (d, J = 14.0, 1H) 3.38 (s, 3H); $^{13}$C NMR 199.3, 198.7, 158.9, 152.9, 152.2, 142.3, 138.9, 137.2, 133.7, 126.1, 124.8, 116.5, 112.0, 107.7, 105.4, 93.0, 60.9, 60.2, 56.0, 55.1, 39.8; MS m/e 596 (M$^+$), 540 (M$^+$-2CO), 512 (M$^+$-3CO), 484 (M$^+$-4CO); HRMS m/e for C$_{25}$H$_{18}$Co$_2$O$_{10}$ calcd. 539.9666 (M$^+$-2CO), found 539.9642.
Hexacarbonyl$\mu^\cdot$$\cdot$$\cdot$-$\eta^4$-(1,2,3-Trimethoxy-5H-dibenzo[a,c]cycloheptyne)dicobalt (9b). Subjecting acetate complex 8b (0.0848 g, 0.135 mmol) to General Procedure C (16 h), followed by flash chromatography (5:1 pet ether:Et$_2$O) afforded 9b (0.0452 g, 59% yield, 66% yield based on recovered starting material) followed by recovered 8b (0.0085 g, 10% recovery). 9b, red-brown solid, mp 116-118°C; IR (KBr) $\nu$ max 2057, 2934, 2090, 2051 cm$^{-1}$; $^1$H NMR 7.69 (dd, J = 7.4, 1.3, 1H), 7.63 (dd, J = 7.6, 1.3, 1H), 7.38 (apparent dt, J = 1.3, 7.4, 1H), 7.35 (apparent dt, J = 1.3, 7.6, 1H), 6.67 (s, 1H), 4.03 (d, J = 14.0, 1H), 3.94 (s, 3H), 3.84 (s, 3H), 3.66 (d, J = 14.0, 1H), 3.39 (s, 3H); $^{13}$C NMR 198.9 (br), 153.1, 152.7, 142.5, 137.7, 137.5, 132.6, 132.4, 132.0, 127.8, 126.4, 126.2, 107.9, 105.7, 92.9, 61.0, 60.4, 56.1, 40.0; MS m/e 538 (M$^+$-1CO), 510 (M$^+$-2CO), 482 (M$^+$-3CO), 454 (M$^+$-4CO), 426 (M$^+$-5CO), 398 (M$^+$-6CO); HRMS m/e for C$_{24}$H$_{16}$Co$_2$O$_9$ calcd. 537.9509 (M$^+$-CO), found 537.9492.

Hexacarbonyl$\mu^\cdot$$\cdot$$\cdot$-$\eta^4$-(9-methoxy-2,4-dimethyl-5H-dibenzo[a,c]cycloheptyne)dicobalt (9c).

Subjecting acetate complex 8c (0.1232 g, 0.207 mmol) to General Procedure C (6 h) gave 9c (0.0938 g, 85% yield), following flash chromatography (50:1 petroleum ether : Et$_2$O), as a brown solid, mp 142-144°C; IR (KBr) $\nu$ max 2924, 2090, 2055, 2025 cm$^{-1}$; $^1$H NMR (-30°C) 7.54 (d, J = 8.5, 1H), 7.21 (d, J = 2.8, 1H), 6.97 - 7.01 (m, 3H), 4.49 (d, J = 14.0, 1H), 3.93 (s, 3H), 3.34 (d, J = 14.0, 1H), 2.50 (s, 3H), 2.29 (s, 3H); $^{13}$C NMR 199.1, 159.4, 140.6, 139.0, 136.20, 136.15, 134.1, 132.2, 132.0, 131.7, 130.0, 116.7, 113.5, 105.2, 92.7, 55.4, 32.9, 21.0, 20.9; MS m/e 534 (M$^+$), 450 (M$^+$-3CO), 394 (M$^+$-5CO); HRMS m/e for C$_{24}$H$_{16}$Co$_2$O$_7$ calcd. 533.9560 (M$^+$), found 533.9569.

Hexacarbonyl$\mu^\cdot$$\cdot$$\cdot$-$\eta^4$-(8-methoxy-4H-benzo[3,4]cycloheptyne[1,2-b]thiophene)dicobalt (9d) and Hexacarbonyl$\mu^\cdot$$\cdot$$\cdot$-$\eta^4$-(8-methoxy-4H-benzo[3,4]cycloheptyne[1,2-c]thiophene)dicobalt (9d').

Subjecting 8d (0.0654 g, 0.114 mmol) to General Procedure C (5 h) afforded 9d/9d' (0.0494 g, 82% yield) following flash chromatography, as an inseparable 45:55 mixture, as a red-brown viscous oil; IR (KBr) $\nu$ max 2937, 2091, 2067, 2045, 1603 cm$^{-1}$; $^1$H NMR for 9d 7.53 (d, J = 8.5, 1H), 7.24 (d, J = 2.8, 1H), 7.18 (d, J = 5.3, 1H), 7.13 (d, J = 5.3, 1H), 6.95 (dd, J = 8.3, 2.8, 1H), 4.25 (s, 2H), 3.900 (s, 3H); for 9d' 7.55 (d, J = 8.5, 1H), 7.28 (d, J = 3.1, 1H), 7.19 (d, J = 2.8, 1H), 7.14 (obscured d, 1H), 6.93 (dd, J = 8.3, 2.8 1H), 4.17 (s, 2H), 3.897 (s, 3H); $^{13}$C NMR 199.0, 159.6, 159.1, 141.3, 139.5, 138.0,
137.2, 136.9, 135.7, 131.1, 130.2, 129.9, 127.1, 127.0, 125.4, 121.9, 121.5, 117.3, 117.1, 114.0, 113.8, 
100.9, 100.4, 92.5, 55.4, 34.8, 33.3; MS m/e 512 (M⁺), 455 (M⁺-2CO), 399 (M⁺-4CO); HRMS m/e for
C₁₂H₁₀Co₂O₇ calcd. 511.8811 (M⁺), found 511.8808.

**Hexacarbonyl[μ-²-(2,3,4,9-tetramethoxy-5H-dibenzo[a,c]cycloheptyne]dicobalt (9e).** Subjecting (8e) (0.6621 g, 1.01 mmol) to General Procedure C (4.5 h) afforded 9e (0.5457 g, 91% yield) following flash chromatography (7:1 petroleum ether:Et₂O), as a red-brown solid; mp 138-140 °C; IR (KBr) ν_max
2938, 2091, 2051, 2023, 1601 cm⁻¹; ¹H NMR  δ 7.47 (d, J = 8.7, 1H), 7.22 (d, J = 2.7, 1H), 6.98 (dd, J = 8.7, 2.7, 1H), 6.67 (s, 1H), 4.03 (v br, 2H), 3.95 (s, 3H), 3.91 (s, 6H), 3.84 (s, 3H); ¹³C NMR 199.1, 159.5, 152.0, 150.1, 141.7, 138.9, 136.1, 131.35, 127.1, 116.8, 113.6, 112.7, 105.6, 92.6, 61.4, 60.9, 56.2, 55.4, 29.4; MS m/e 596 (M⁺), 568 (M⁺-CO), 540 (M⁺-2CO), 512 (M⁺-3CO), 484 (M⁺-4CO), 456 (M⁺-5CO); HRMS for C₂₅H₁₈Co₂O₁₁ (M⁺) calcd. 595.9564, found 595.9548.

**Hexacarbonyl[μ-²-(1,2,3,8,9-pentamethoxy-5H-dibenzo[a,c]cycloheptyne]dicobalt (9f).** Subjecting (8f) (0.9250 g, 1.35 mmol) to General Procedure C (4.5 h) afforded 9f (0.7021 g, 83% yield) following flash chromatography (5:1 hexanes:Et₂O), as a dark brown solid, mp 115-117 °C; IR (KBr) ν_max
2939, 2090, 2054, 1593 cm⁻¹; ¹H NMR  δ 7.30 (d, J = 8.7, 1H), 6.97 (d, J = 8.7, 1H), 6.63 (s, 1H), 3.99 (d, J = 14.0, 1H), 3.99 (s, 3H), 3.95 (s, 3H), 3.92 (s, 3H), 3.81 (s, 3H), 3.67 (d, J = 14.0, 1H), 3.40 (s, 3H); ¹³C NMR 199.5, 153.1, 152.3, 152.0, 148.4, 142.3, 137.3, 132.2, 128.3, 126.3, 125.9, 110.6, 107.5, 107.3, 85.8, 60.7, 60.7, 60.4, 56.1, 55.8, 40.3; MS m/e 626 (M⁺), 598 (M⁺-CO), 570 (M⁺-2CO), 542 (M⁺-3CO), 514 (M⁺-4CO), 486 (M⁺-5CO), 458 (M⁺-6CO); HRMS for C₂₆H₂₀Co₂O₁₁ (M⁺) calcd. 625.9670, found 625.9673.

**Hexacarbonyl[μ-²-(5H-dibenzo[a,c]cycloheptyne]dicobalt (9g).** Subjecting 8g (0.0604 g, 0.127 mmol) to General Procedure C (16 h) afforded 9g (0.0311, 58% yield) following flash chromatography (100% petroleum ether), as a dark brown solid, mp 130-132 °C; IR (KBr) ν_max
3059, 2959, 1688, 2091, 2052, 2022 cm⁻¹; ¹H NMR  δ 7.71 (m, 1H), 7.59 (s, 1H), 7.40-7.47 (m, 3H), 7.28-7.36 (m, 3H), 4.05 (s, 2H); ¹³C NMR 199.0, 140.4, 140.2, 138.5, 137.3, 133.2, 132.1, 130.4, 128.6, 128.3, 127.92, 127.86,
127.5, 104.2, 92.0, 39.9; MS m/e 420 (M+ -2CO), 336 (M+ -5CO), 308 (M+ -6CO); HRMS m/e for C_{21}H_{10}Co_{2}O_{6} calcd. 447.9192 (M+ -CO), found 447.9214.

**Hexacarbonyl[µ-₄-(9-carbomethoxy-1,2,3-trimethoxy-5H-dibenzo[a,c]cycloheptene)dicobalt**

(9h); Subjecting (8h) (0.2304 g, 0.351 mmol) to General Procedure C (5 h) afforded 9h (0.1831 g, 84% yield) following flash chromatography (5:1 petroleum ether:Et₂O), as a dark brown viscous oil; IR (KBr) max 2952, 2092, 2055, 2023, 1730 cm⁻¹; ¹H NMR 8.30 (d, J = 1.9, 1H), 7.98 (dd, J = 8.2, 1.9, 1H), 7.69 (d, J = 8.2, 1H), 6.67 (s, 1H), 4.05 (d, J = 14.1, 1H), 3.98 (s, 3H), 3.95 (s, 3H), 3.84 (s, 3H), 3.65 (d, J = 14.1, 1H), 3.39 (s, 3H); ¹³C NMR 198.7, 166.7, 153.24, 153.15, 142.4, 138.3, 137.9, 137.0, 132.9, 129.4, 126.8, 125.5, 107.9, 105.4, 91.4, 61.1, 60.6, 56.1, 52.3, 39.9; MS m/e 596 (M+ -1CO), 568 (M+ -2CO), 540 (M+ -3CO), 512 (M+ -4CO), 484 (M+ -5CO); HRMS for C_{26}H_{18}Co_{2}O_{11} (M+ -3CO) calcd. 539.9666, found 539.9683.

**1,2,3,9-Tetramethoxy-5H-dibenzo[a,c]cycloheptene (17a).** To a solution of 9a (0.0782 g, 0.131 mmol) in degassed 1,2-dichloroethane (2 mL) was added bis(trimethylsilyl)acetylene (62 µL, 0.274 mmol) and triethylsilane (0.10 mL, 0.63 mmol). The mixture was heated to 65 °C for 6 h and cooled to room temperature, at which point trifluoroacetic acid (0.5 mL) was added. After stirring for an additional 12 h, the mixture was subjected to a conventional extractive workup. Preparative TLC (4:1 hexanes : Et₂O) afforded 17a (0.0396 g, 97% yield) as a colorless solid, mp 102-3 °C (MeOH), Lit.²⁹ 102-3 °C (MeOH).

**2,3,4,9-Tetramethoxy-5H-dibenzo[a,c]cycloheptene (17e).** To a solution of 9e (0.3492 g, 0.586 mmol) in degassed 1,2-dichloroethane (20 mL) was added bis(trimethylsilyl)acetylene (0.27 mL, 1.2 mmol) and triethylsilane (0.47 mL, 2.9 mmol). The mixture was heated to 65 °C for 6 h and cooled to room temperature, at which point trifluoroacetic acid (1.0 mL) was added. After stirring for an additional 12 h, the mixture was subjected to a conventional extractive workup. Preparative TLC (10:1 petroleum ether : Et₂O) afforded 17e (0.1718 g, 94% yield) as a colorless viscous oil; IR (KBr) max 2936, 1604 cm⁻¹; ¹H NMR 7.61 (d, J = 8.7, 1H), 6.95 (dd, J = 8.7, 2.6, 1H), 6.85 (d, J = 2.6, 1H), 6.82 (s, 1H), 6.57 (d, J = 10.0, 1H), 6.26 (m, 1H), 3.94 (s, 3H), 3.93 (s, 3H), 3.90 (s, 3H), 3.89 (s, 3H), 2.47 (v br,
1,2,3,8,9-Pentaamethoxy-5H-dibenzo[a,c]cycloheptene (17f). To a solution of 9f (0.0945 g, 0.151 mmol) in degassed 1,2-dichloroethane (2 mL) was added bis(trimethylsilyl)acetylene (62 µL, 0.32 mmol) and triethylsilane (0.12 mL, 0.76 mmol). The mixture was heated to 65 °C for 6 h and cooled to room temperature, at which point trifluoroacetic acid (0.5 mL) was added. After stirring for an additional 12 h, the mixture was subjected to a conventional extractive workup. Preparative TLC (7:1 petroleum ether : Et₂O) afforded 17f (0.0465 g, 90% yield) as a colorless solid, mp 163-165 °C; IR (KBr) ν max 3036, 2926, 1573 cm⁻¹; ¹H NMR δ 7.55 (d, J = 8.7, 1H), 6.94 (d, J = 8.7, 1H), 6.78 (d, J = 10.1, 1H), 6.58 (s, 1H), 6.29 (m, 1H), 3.95 (s, 3H), 3.91 (s, 3H), 3.90 (s, 3H), 3.48 (s, 3H), 3.06 (dd, J = 12.9, 7.9, 1H), 2.80 (ddd, J = 12.9, 5.9, 1.8, 1H); ¹³C NMR 152.3, 150.4, 145.2, 140.7, 140.1, 132.2, 131.1, 128.3, 127.5, 124.0, 123.8, 109.9, 105.6, 61.0, 60.6, 55.9, 55.8, 33.5; MS m/e 342 (M⁺); HRMS for C₂₀H₂₂O₅ calcd. 342.1467, found 342.1475.

9-Carbomethoxy-1,2,3-trimethoxy-5H-dibenzo[a,c]cycloheptene (17h). To a solution of 9h (0.1831 g, 0.293 mmol) in degassed 1,2-dichloroethane (7 mL) was added bis(trimethylsilyl)acetylene (0.14 mL, 0.59 mmol) and triethylsilane (0.23 mL, 0.14 mmol). The mixture was heated to 65 °C for 6 h and cooled to room temperature, at which point trifluoroacetic acid (3.0 mL) was added. After stirring for an additional 12 h, the mixture was subjected to a conventional extractive workup. Preparative TLC (5:1 hexanes : Et₂O) afforded 17h (0.0.0789 g, 79% yield) as a colorless solid, mp 85-86 °C; IR (KBr) ν max 2950, 1722, 1594 cm⁻¹; ¹H NMR 8.03 (s, 1H), 7.91 (1/2 AB quartet, J = 8.3, 1H), 7.89 (1/2 AB quartet, J = 8.3, 1H), 6.62 (d, J = 10.0, 1H), 6.59 (s, 1H), 6.29 (m, 1H), 3.96 (s, 3H), 3.92 (s, 3H), 3.90 (s, 3H), 3.46 (s, 3H), 3.08 (m, 1H), 2.75 (m, 1H); ¹³C NMR 167.0, 153.3, 152.3, 140.8, 140.5, 139.4, 136.5, 133.2, 132.0, 130.1, 128.8, 127.6, 125.4, 123.3, 105.8, 61.1, 60.7, 55.9, 52.1, 33.3; MS m/e 340 (M⁺); HRMS for C₂₀H₂₀O₄ (M⁺) calcd. 340.1311, found 340.1306.
6,7-Dihydro-3,9,10,11-tetramethoxy-5H-dibenzo[a,c]cyclohepten-5-one (18a). To a solution of alkene 17a (0.0521 g, 0.167 mmol) in THF (7 mL) at 0 °C was added BH₃-THF (0.75 mL of a 1M solution). The cooling bath was removed, and the reaction stirred at room temperature for 12 h. NaOH (1 mL of a 10% aqueous solution) and H₂O₂ (1 mL of a 33% aqueous solution) were added, and the mixture stirred for 4 h, followed by warming to 40 °C for 0.5 h. A conventional workup gave a crude alcohol which was added slowly as a solution in CH₂Cl₂ to a -78 °C solution prepared from the addition of DMSO (0.14 mL, 2.0 mmol) to oxalyl chloride (86 µL, 1.0 mmol) in CH₂Cl₂ (10 mL) at -78 °C. Diisopropylethylamine (0.70 mL, 4.0 mmol) was added and the solution allowed to come to room temperature over 6h. A conventional workup gave a residue with a 96:4 mixture of ketone regioisomers (by integration of relevant 1H NMR resonances); preparative TLC (1:1 hexanes : Et₂O) afforded 18a (0.0440, 80% yield) as a colorless solid, mp 141-2 °C (hexanes), lit. 142-3 °C (MeOH), 140.5-141 °C, 135-6 °C.¹¹

6,7-Dihydro-3,8,9,10-tetramethoxy-5H-dibenzo[a,c]cyclohepten-5-one. (18e). To a solution of alkene 17e (0.1793 g, 0.574 mmol) in THF (20 mL) at 0 °C was added BH₃-THF (2.7 mL of a 1M solution). The cooling bath was removed, and the reaction stirred at room temperature for 12 h. NaOH (3 mL of a 10% aqueous solution) and H₂O₂ (3 mL of a 33% aqueous solution) were added, and the mixture stirred for 4 h, followed by warming to 40 °C for 0.5 h. A conventional workup gave a crude alcohol which was dissolved in CH₂Cl₂ (20 mL). To this solution was added PDC (0.55 g), and the mixture was stirred for 12 h. A conventional workup followed by preparative TLC (3:1 petroleum ether:Et₂O) afforded 18e (0.1291 g, 68% yield) as a colorless solid, mp 123-125 °C; IR (KBr) νmax 2937, 1681, 1601 cm⁻¹; ¹H NMR 7.36 (m, 1H), 7.14 (s, 1H), 7.13 (obsurred m, 1H), 6.69 (s, 1H), 3.92 (s, 3H), 3.89 (s, 3H), 3.88 (s, 6H), 2.97-3.00 (m, 2H), 2.92-2.94 (m, 2H); ¹³C NMR 206.3, 158.9, 152.2, 150.1, 141.6, 139.7, 134.4, 131.4, 130.5, 125.4, 118.8, 112.1, 109.0, 61.3, 60.8, 56.0, 55.4, 47.3, 20.4; MS m/e 328 (M⁺); HRMS for C₁₉H₂₀O₅ (M⁺) calcd. 328.1311, found 328.1322.

6,7-Dihydro-3,4,9,10,11-pentamethoxy-5H-dibenzo[a,c]cyclohepten-5-one (18f). To a solution of alkene 17f (0.2175 g, 0.636 mmol) in THF (25 mL) at 0 °C was added BH₃-THF (3.0 mL of a 1M
solution). The cooling bath was removed, and the reaction stirred at room temperature for 12 h. NaOH (3 mL of a 10% aqueous solution) and H$_2$O$_2$ (3 mL of a 33% aqueous solution) were added, and the mixture stirred for 4 h, followed by warming to 40 °C for 0.5 h. A conventional workup gave a crude alcohol which was dissolved in CH$_2$Cl$_2$ (20 mL). To this solution was added PDC (0.55 g), and the mixture was stirred for 12 h. A conventional workup followed by preparative TLC (3:1 petroleum ether:Et$_2$O) afforded 18f (0.1505 g, 67% yield) as a colorless solid, mp 164-165 °C, lit. 156-157 °C; $^{22}$IR (KBr) $\nu_{max}$ 2939, 1701, 1598 cm$^{-1}$; $^1$H NMR  7.26 (d, J = 8.6, 1H), 7.00 (d, J = 8.6, 1H), 6.56 (s, 1H), 3.91 (s, 3H), 3.87 (s, 3H), 3.86 (s, 6H), 3.57 (s, 3H), 2.97-3.05 (m, 2H), 2.85 (m, 1H), 2.59 (m, 1H); $^{13}$C NMR 204.8, 152.6, 151.8, 151.7, 144.3, 141.4, 135.24, 135.21, 126.24, 126.16, 123.8, 113.0, 107.5, 62.2, 61.0, 60.8, 55.9, 55.8, 49.6, 30.1; MS m/e 354 (M$^+$); HRMS for C$_{20}$H$_{22}$O$_6$ (M$^+$) calcd. 358.1416, found 358.1402.

6,7-Dihydro-3-carbomethoxy-9,10,11-trimethoxy-5H-dibenzo[a,c]cyclohepten-5-one (18h). To a solution of alkene 17h (0.0307 g, 0.0902 mmol) in THF (5 mL) at 0 °C was added BH$_3$-THF (0.45 mL of a 1M solution). The cooling bath was removed, and the reaction stirred at room temperature for 12 h. NaOH (1 mL of a 10% aqueous solution) and H$_2$O$_2$ (1 mL of a 33% aqueous solution) were added, and the mixture stirred for 4 h, followed by warming to 40 °C for 0.5 h. A conventional workup gave a crude alcohol which was dissolved in CH$_2$Cl$_2$ (10 mL). To this solution was added PDC (0.5 g), and the mixture was stirred for 12 h. A conventional workup followed by preparative TLC (3:1 petroleum ether:Et$_2$O) afforded 18h (0.0.0260 g, 81% yield) as a colorless solid, mp 144-145 °C; lit.$^4$ 144.2-144.8 °C.

(5R)- 6,7-Dihydro-3,9,10,11-tetramethoxy-5H-dibenzo[a,c]cyclohepten-5-ol (19a). A suspension of 3 -nitrophenylboronic acid (0.334 g, 2.0 mmol), L-tartaric acid (0.0300 g, 2.0 mmol) and CaH$_2$ (0.168 g, 4.0 mmol) in THF (5 mL) was heated to reflux for 1h. After cooling and allowing the solids to settle, the supernatant solution (2.5 mL, ca. 1 mmol) was added to ketone 18a (0.0634 g, 0.193 mmol). Lithium borohydride (0.5 mL of a 2M solution, 1.0 mmol) was added over a period of 5 min, and the solution stirred for 0.5 h. NaOH (1 mL of a 10% aqueous solution) and water (2 mL) were added, and
the reaction subjected to a conventional extractive workup. Preparative TLC (2:1 pet ether:Et$_2$O) afforded 19a (0.0610 g, 96%), 95% ee (Chiralcel OD-H, i-PrOH-hexanes), mp 137-9 °C (CH$_2$Cl$_2$:pet ether) [ $\alpha$ ]$_D$ 120° (c 0.0144); $^1$H NMR (DMSO-d$_6$) 7.24 (d, J = 8.4, 1H), 7.17 (d, J = 2.8, 1H), 6.85 (dd, J = 84, 2.8, 1H), 6.75 (s, 1H), 5.23 (d, J = 4.7, 1H), 4.27 (m, 1H), 3.82 (s, 3H), 3.80 (s, 3H), 3.75 (s, 3H), 3.48 (s, 3H), 2.32-2.45 (m, 2H), 2.06 (m, 1H), 1.73 (m, 1H); $^{13}$C NMR (DMSO-d$_6$) 158.3, 151.9, 150.2, 144.5, 140.4, 135.2, 130.3, 124.9, 124.0, 111.2, 108.7, 107.9, 68.1, 60.5, 60.4, 55.8, 54.9, 41.3, 29.9; HRMS m/e for C$_{19}$H$_{22}$O$_5$ calcd. 330.1467 (M$^+$), found 330.1479.

(5R)- 6,7-Dihydro-3,8,9,10-tetramethoxy-5H-dibenzo[a,c]cyclohepten-5-ol (19e). A suspension of 3-nitrophenylboronic acid (0.334 g, 2.0 mmol), L-tartaric acid (0.0300 2.0 mmol) and CaH$_2$ (0.168 g, 4.0 mmol) in THF (5 mL) was heated to reflux for 1 h. After cooling and allowing the solids to settle, the supernatant solution (2.5 mL, ca. 1 mmol) was added to ketone 18e (0.0217 g, 0.0661 mmol). Lithium borohydride (0.2 mL of a 2 M solution, 0.4 mmol) was added over a period of 1.5 h, and the solution stirred for 0.5 h. NaOH (1 mL of a 10% aqueous solution) and water (2 mL) were added, and the reaction subjected to a conventional extractive workup. Preparative TLC (1:1 petroleum ether:Et$_2$O) afforded 19e (0.0213 g, 98%), 98% ee (Chiralcel AS-H, 10% i-PrOH-hexanes) as a viscous oil, [ $\alpha$ ]$_D$ 102° (c 0.533); IR (KBr) $\nu_{max}$ 3500 br, 2936, 1646 cm$^{-1}$; $^1$H NMR (DMSO-d$_6$) 7.30 (d, J = 8.5, 1H), 7.18 (d, J = 2.5, 1H), 6.91 (dd, J = 8.5, 2.5, 1H), 5.25 (d, J = 4.5, 1H), 3.83 (s, 3H), 3.81 (s, 3H), 3.79 (s, 3H), 3.78 (s, 3H), 2.86 (m, 1H), 2.38 (m, 3H), 1.75-1.86 (m, 2H); $^{13}$C NMR (CDCl$_3$) 159.4, 151.7, 150.8, 143.2, 141.3, 135.4, 130.3, 129.0, 125.0, 112.5, 108.7 (br), 107.9, 70.7 (br), 61.6, 61.0, 55.1, 55.4, 41.5, 21.5; MS m/e 330 (M$^+$); HRMS for C$_{19}$H$_{22}$O$_5$ (M$^+$) calcd. 330.1467, found 330.1481.

(5S)- 5-Azido-6,7-dihydro-3,9,10,11-tetramethoxy-5H-dibenzo[a,c]cycloheptene (20a). To a suspension of alcohol 19a (0.0583 g, 0.176 mmol), Zn(N$_3$)$_2$-(pyridine)$_2$ (0.0810 g, 0.264 mmol), and triphenylphosphine (0.185 g, 0.704 mmol) in toluene (2 mL) was added diisopropyl azodicarboxylate (0.14 mL, 0.70 mmol) in a dropwise fashion. After stirring for 4h, the mixture was filtered through a plug of silica gel, and concentrated under reduced pressure. Preparative TLC (4:1 hexanes:Et$_2$O) afforded 20a contaminated by 10% of alkene 17a (0.0440 g, 64% of 20a, 7% of 17a). Repeated
preparative TLC (10:1 hexanes : EtOAc) afforded pure 20a as a viscous oil, [α]<sub>D</sub> 22 110° (c 0.0100) (93% ee material as evaluated on 2), IR (KBr) ν<sub>max</sub> 2936, 2013 cm<sup>-1</sup>; ¹H NMR (major atropisomer, 91%) 7.42 (d, J = 8.5, 1H), 7.13 (d, J = 2.5, 1H), 6.92 (dd, J = 8.5, 2.5, 1H), 6.60 (s, 1H), 4.44 (dd, J = 11.5, 7.0, 1H), 3.92 (s, 6H), 3.90 (s, 3H), 3.65 (s, 3H), 2.45-2.60 (m, 2H), 2.33 (m, 1H), 2.00 (m, 1H); resonances from the minor atropisomer (9%) could be observed at 7.42 (d, J = 8.8, 1H), 6.97 (dd, J = 8.8, 2.6, 1H), 6.81 (d, J = 2.6, 1H), 6.58 (s, 1H), 4.71 (d, J = 6.8, 1H), 3.93 (s, 3H), 3.88 (s, 3H), 3.62 (s, 3H); ¹³C NMR 159.0, 152.6, 150.9, 141.2, 138.6, 134.7, 131.7, 126.0, 124.3, 112.5, 109.2, 107.6, 61.1, 61.0, 60.8, 56.0, 55.3, 38.9, 30.4; MS m/e 355 (M⁺); HRMS m/e for C₁₉H₂₁N₃O₄ calcd. 355.1532 (M⁺), found 355.1541.

(S)- N-Acetyl-O-methyl-colchicinol, (NSC 51046) (2). To a solution containing azide 20a with 10% alkene 17a (0.0186 g, 48.1 µmol 20a) in 100% EtOH saturated with H₂ was added Lindlar catalyst (0.0068 g). The mixture was stirred under H₂ for 20h, filtered through Celite® and concentrated under reduced pressure. The residue was dissolved in CH₂Cl₂, cooled to 0 °C, and acetic anhydride (0.2 mL) and pyridine (0.2 mL) were added. The mixture was allowed to stir 12 h with gradual warming to room temperature. Concentration under reduced pressure, followed by preparative TLC (19:1 CH₂Cl₂ : MeOH) afforded 2 (0.0157 g, 88% yield), which was spectroscopically identical with authentic material,¹¹ 93% ee (Chiralcel OD-H, 10% i-PrOH-hexanes). A single recrystallization afforded 2 of > 99% ee, mp 203-4 °C (CH₂Cl₂/hexanes); lit. ¹b 204-5 °C (CH₂Cl₂/hexanes); [α]<sub>D</sub> 24 -64° (c 0.0056, CHCl₃); lit. ¹b [α]<sub>D</sub> 20 -65° (c 0.46, CHCl₃); lit. ¹a [α]<sub>D</sub> 20 -64.9° (c 1.03%, CHCl₃); ¹H NMR (DMSO-d₆) 8.34 (d, J = 8.6, 1H), 7.25 (d, J = 8.4, 1H), 6.91 (d, J = 2.6, 1H), 6.87 (dd, J = 8.4, 2.6, 1H), 6.76 (s, 1H), 4.52 (m, 1H), 3.83 (s, 3H), 3.79 (s, 3H), 3.78 (s, 3H), 3.47 (s, 3H), 2.48 (m, 1H, obscured), 2.15 (m, 1H), 2.07 (m, 1H), 1.88 (s, 3H), 1.85 (m, 1H); ¹³C NMR (DMSO-d₆) 168.2, 158.3, 152.1, 150.3, 141.8, 140.5, 134.7, 130.5, 126.1, 124.3, 110.7, 109.4, 108.1, 60.50, 60.45, 55.8, 54.9, 48.1, 30.1, 22.6.

(5S)- 5-Azido-6,7-dihydro-3,8,9,10-tetramethoxy-5H-dibenzo[a,c]cycloheptene (20e). To a suspension of 19e (0.0346 g, 0.105 mmol), Zn(N₃)₂-2pyridine (0.0484 g, 0.157 mmol), and triphenylphosphine (0.1099 g, 0.419 mmol) in toluene (3 mL) was added diisopropyl azodicarboxylate
(81 µL, 0.42 mmol) in a dropwise fashion. After stirring for 4 h, the mixture was filtered through a plug of silica gel, and concentrated under reduced pressure. Preparative TLC (4:1 hexanes:EtOAc) afforded 20e (0.0286 g, 77% yield) as a viscous oil; [α]D24 -126° (c 0.663, CHCl3) (95% ee material as evaluated on 21); IR (KBr) νmax 2937, 2095 cm⁻¹; ¹H NMR 7.31 (d, J = 8.4, 1H), 7.12 (br s, 1H), 6.94 (dd, J = 8.4, 2.7, 1H), 6.70 (s, 1H), 4.46 (m, 1H), 3.94 (s, 3H), 3.91 (s, 3H), 3.905 (s, 3H), 3.900 (s, 3H), 3.01 (br m, 1H), 2.55 (m, 1H), 2.06 (m, 2H); ¹³C NMR (DMSO-d₆) 158.8, 151.6, 150.3, 141.0, 138.0, 134.7, 130.7, 129.9, 123.4, 112.8, 110.6 (br), 108.2, 61.4, 61.2, 60.4, 55.8, 55.2, 38.1, 21.3; MS m/e 355 (M⁺); HRMS for C₁₉H₂₁N₃O₄ (M⁺) calcd. 355.1532, found 355.1537.

(5S)- 5-Acetamido-6,7-dihydro-3,8,9,10-tetramethoxy-5H-dibenzo[a,c]cycloheptene (21). To a solution containing azide 20e with (0.0286 g, 80.5 µmol) in 100% EtOH (10 mL) saturated with H₂ was added Lindlar catalyst (0.0109 g). The mixture was stirred under H₂ for 20 h, filtered through Celite® and concentrated under reduced pressure. The residue was dissolved in CH₂Cl₂ (10 mL), cooled to 0 °C, and acetic anhydride (0.2 mL) and pyridine (0.2 mL) were added. The mixture was allowed to stir 12 h with gradual warming to room temperature. Concentration under reduced pressure, followed by preparative TLC (19:1 CH₂Cl₂ : MeOH) afforded 21 (0.0237 g, 79% yield) 95% ee (Chiralcel OD-H, 10% i-PrOH-hexanes). A single recrystallization afforded 21 of > 99% ee, as colorless crystals, mp 186-188 °C (Et₂O/hexanes); [α]D²² -52.4° (c 0.783, CHCl₃); IR (KBr) νmax 3288 br, 2936, 1664 cm⁻¹; ¹H NMR (DMSO-d₆) 8.41 (d, J = 8.4, 1H), 7.32 (d, J = 8.1, 1H), 6.88-6.94 (m, 2H), 6.79 (s, 1H), 4.51 (m, 1H), 3.85 (s, 3H), 3.79 (s, 6H), 3.78 (s, 3H), 2.91 (dd, J = 13.2, 6.0, 1H), 2.16 (m, 1H), 1.95 (m, 1H), 1.89 (s, 3H), 1.78 (m, 1H); ¹³C NMR (DMSO-d₆) 168.6, 158.9, 151.6, 150.4, 141.4, 140.9, 135.3, 130.9, 129.3, 123.7, 111.3, 110.1, 108.3, 61.5, 60.4, 55.9, 55.1, 48.4, 22.7, 21.9; (a resonance at 40.0 in CDCl₃ is obscured in DMSO-d₆); MS m/e 371 (M⁺); HRMS for C₂₁H₂₅NO₅ (M⁺) calcd. 371.1733, found 371.1740.

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Supporting Information Available. \(^1\)H and \(^{13}\)C spectra for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

References


(25) Rapid addition of LiBH$_4$ afforded 19b in ca. 50% ee.


